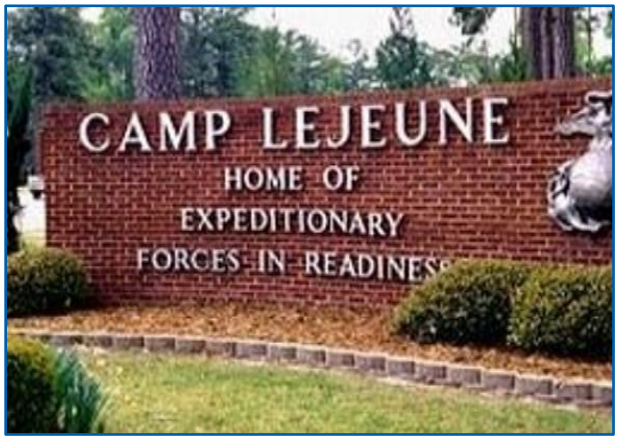
Exhibit 3

ATSDR Assessment of the Evidence for the Drinking Water Contaminants at Camp Lejeune and Specific Cancers and Other Diseases



January 13, 2017

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Overview

The Agency for Toxic Substances and Disease Registry (ATSDR) has a unique mandate under the Superfund laws to assess the presence and nature of health hazards at specific Superfund sites, to help prevent or reduce further exposure and the illnesses that result from such exposures, and to expand the knowledge base about health effects from exposure to hazardous substances. As part of its mandate, ATSDR has completed several epidemiological studies to determine if Marines, Navy personnel and civilians residing and working on U.S. Marine Corps Base Camp Lejeune were at increased risk for certain health effects as a result of exposure to water contaminated with volatile organic compounds (VOCS). These studies, two retrospective cohort mortality studies of Marines/Navy personnel and of civilian workers, and a case-control study of male breast cancer among Marines (Bove et al. 2014a, Bove et al. 2014b, Ruckart et al. 2015), used data from extensive water modeling (Maslia et al. 2007, 2013) to reconstruct monthly levels of contaminants in the drinking water. These contaminants included trichloroethylene (TCE), tetrachloroethylene (PCE), benzene, 1,2-dichloroethylene (DCE) and vinyl chloride. The two cohort studies found elevated risks for several cancers, including cancers of the kidney, rectum, prostate, lung, leukemias and multiple myeloma, when compared to similar unexposed cohorts from U.S. Marine Corps Base Camp Pendleton. Parkinson disease was elevated among civilian workers at Camp Lejeune but could not be evaluated in the study of Marines/Navy personnel due to small numbers. Findings from the case-control study suggested possible associations between male breast cancer and being stationed at Camp Lejeune and cumulative exposure to the contaminated drinking water but the study was limited by the small number of cases in the higher exposure categories.

ATSDR integrated the findings from its Camp Lejeune studies with findings from studies of other populations exposed occupationally or environmentally to the chemicals detected in the drinking water at Camp Lejeune: trichloroethylene (TCE), tetrachloroethylene (also known as perchloroethylene or PCE), vinyl chloride and benzene. The purpose was to assess the strength of the evidence supporting causality of adverse health effects from exposures to the drinking water contaminants at Camp Lejeune. This report represents ATSDR's assessment of the state of evidence at this time.

For this assessment, ATSDR did not conduct any new meta-analyses. Instead, ATSDR reviewed the scientific literature on these contaminants and placed high weight on assessments conducted by other agencies mandated to evaluate the health effects of these chemicals: i.e., the U.S. Environmental Protection Agency (EPA 2011, 2012), the National Toxicology Program (NTP 2015) and the International Agency for Research on Cancer (IARC 100F, 2012; 106, 2014). High weight was also given to meta-analyses conducted by EPA (Scott and Jinot 2011) and other researchers. This report summarizes the evidence for 16 diseases for which there was at least some epidemiological evidence for an association with either TCE or PCE, the primary contaminants in the drinking water systems at Camp Lejeune. The report also assesses the evidence linking these diseases with vinyl chloride and benzene. **Two additional diseases, lung cancer and cervical cancer, are not included in this report. ATSDR is currently updating its assessment of these two cancers and will publish the assessment at a later date.**

Background

The Hadnot Point treatment plant provided drinking water to the main portion of the base at Camp Lejeune, including most of the barracks and workplaces. Samples of the Hadnot Point distribution system were conducted by the base in May and July 1982, December 1984, and throughout 1985. During the 1982 sampling, measured levels of TCE and PCE in the distribution system of Hadnot Point were as high as 1,400 ppb and 100 ppb, respectively. Vinyl chloride and benzene were also detected in the Hadnot Point distribution system during sampling conducted on or after December 1984. The Tarawa Terrace treatment plant provided drinking water to the Tarawa Terrace housing area at the base. Samples of the Tarawa Terrace distribution system were conducted by the base in May and July 1982, and February 1985 onward. During the July 1982 distribution system sampling, PCE was measured as high as 104 ppb and reached a maximum of 215 ppb during the February 1985 sampling.

The current U.S. maximum contaminant levels (MCLs) for TCE and PCE are 5 ppb. The MCLs for vinyl chloride and benzene are 2 ppb and 5 ppb, respectively. The MCLs for TCE, vinyl chloride and benzene were in effect as of 1989, and the MCL for PCE was in effect as of 1992. Historical reconstruction modeling of the drinking water contamination indicated that TCE and PCE levels above their current MCLs were likely present in the distribution systems since the 1950s. The highly contaminated supply wells serving these systems were shut down by February 1985. For the retrospective cohort study of Marines and Navy personnel at Camp Lejeune, the relevant exposure period was 1975 – January 1985. The estimated monthly average contaminant concentrations in the Hadnot Point and Tarawa Terrace systems during this period are shown in tables in the appendix of this report. In the Hadnot Point system, the median monthly estimated average concentrations of TCE, PCE, vinyl chloride and benzene was 366 ppb, 15 ppb, 22 ppb and 5 ppb, respectively. In the Tarawa Terrace system, the median monthly estimated average concentrations of PCE, TCE and vinyl chloride were 85 ppb, 4 ppb and 6 ppb. The median number of months a marine or Navy personnel was stationed at the base was 18 months.

A marine in training at Camp Lejeune consumes an estimated 6 liters of water per day for three days per week and 3 liters per day the rest of the week (ATSDR 2016). Under warm weather conditions, a marine may consume between 1 and 2 quarts of water per hour and shower twice a day (Bove et al. 2014a). It is likely that during training, the water supplied in the field came from the Hadnot Point water system with both measured and estimated levels of TCE and PCE substantially higher than their MCLs.

Methods

Description of the candidate list of diseases

The selection of diseases for assessment was initially based on a previous review of the literature that was included in a feasibility assessment for the mortality studies at Camp Lejeune (Bove and Ruckart 2008). That literature review identified a list of diseases for which there was at least limited or suggestive evidence of an association with exposures to TCE or PCE. Limited or suggestive evidence was considered to have occurred when a positive association (e.g., an effect estimate such as the relative

risk or the odds ratio is greater than 1.0) was observed in at least one epidemiological study of high quality (i.e., the effect of biases on the study's findings was probably low and the precision of the effect estimate was adequate, e.g., the width of the 95% confidence interval as measured by the ratio of the upper to lower limit is ≤ 3) but there were inconsistencies in the results across studies and there was substantial doubt that the body of evidence is strong enough to rule out the effect of biases. This definition of limited/suggestive evidence is similar to that used by the Institute of Medicine (IOM, now renamed the Health And Medicine Division of the National Academies of Sciences, Engineering, and Medicine) (IOM 2008). The list of diseases included cancers of the kidney, liver, cervix, bladder, lung, breast, pancreas, esophagus, non-Hodgkin lymphoma, Hodgkin disease, leukemias, multiple myeloma, and several non-cancers including scleroderma, Parkinson disease, liver disease, kidney disease, generalized skin disorder, lupus, and spontaneous abortion.

After review of the assessments of TCE and PCE by EPA (EPA 2011, 2012; Chiu et al. 2013; Guyton et al. 2014), IARC (IARC 106, 2014) and NTP (NTP 2015), ATSDR added cancers of the brain and prostate and cardiac congenital malformations to its list of diseases with some association with either TCE or PCE exposure. Finally, the list was expanded to include rectal cancer and kidney diseases based on the findings from the Camp Lejeune mortality studies and studies of PCE-contaminated drinking water at Cape Cod MA (Paulu et al. 1999). For this assessment, ATSDR decided to focus on sixteen of these diseases: cancers of the kidney, hematopoietic system (leukemias, non-Hodgkin lymphoma, and multiple myeloma), liver, pancreas, prostate, breast, bladder, esophagus, rectum and brain, and Parkinson disease, kidney disease, scleroderma and cardiac congenital malformations. In future assessments, ATSDR will evaluate the remaining list of diseases as well as add new diseases to the list if future research indicates an association with TCE or PCE exposure.

Literature search

Reviews of epidemiological studies involving TCE and PCE exposure have been conducted by EPA (2011), IARC (2014) and NTP (2015). In addition, meta-analyses have recently been conducted by NCI researchers (Karami et al. 2012, Karami et al. 2013), EPA (EPA 2011, summarized in Scott and Jinot 2011), and an IARC workgroup (Vlaanderen et al. 2014) for TCE and kidney cancer, hematopoietic cancers and liver cancer, and PCE and bladder cancer. ATSDR utilized these reviews and meta-analyses to identify epidemiological studies for TCE and PCE. Meta-analyses of benzene and hematopoietic cancers (Khalade et al. 2010, Vlaanderen et al. 2011, 2012) were used to identify epidemiological studies for benzene. For vinyl chloride, we reviewed the IARC monograph 100F (2012) that evaluated vinyl chloride to identify epidemiological studies involving vinyl chloride exposure.

In addition, literature searches using PubMed were conducted to identify epidemiological studies conducted after each of the meta-analyses and reviews were completed. The keywords used in the search were the combination of each of the contaminants and each of the diseases being assessed. An additional search was conducted using the keyword "chlorinated solvents" in combination with each of the diseases being assessed. The PubMed search identified epidemiological studies published through September 4, 2015. Subsequently a PubMed search was conducted to identify epidemiological studies published through August 12, 2016. All meta-analyses that evaluated epidemiological studies were identified either from the reports by IARC, EPA and NTP or by the literature search and are included in this assessment. All epidemiological studies that were published after these reports and meta-analyses

were conducted were identified by the literature search and included in this assessment. Epidemiological studies that evaluated exposure-response relationships, whether included in a meta-analysis or not, were included in this assessment. Also identified by the literature search and considered in this assessment were published articles that reviewed the epidemiological evidence for the chemicals and diseases assessed in this document.

A literature search was not conducted for animal studies. Instead, information from animal studies, and information on possible disease mechanisms, were obtained from a review of the EPA, IARC and NTP reports and published articles that reviewed the epidemiological evidence. Information on animal studies and mechanism were also obtained from the epidemiological studies identified via the literature search or that were included in the meta-analyses.

Classification of Evidence

Several classification systems have been develop to reflect the strength of the evidence for a causal relationship between an exposure and a particular health effect (IOM 2012). The IARC, EPA and NTP have established classification systems for exposures that may pose a cancer hazard. The Institute of Medicine has adopted classification systems to evaluate non-cancer endpoints as well as cancers. These classification systems were developed under different mandates and therefore differ in their approach to the evidence (IOM 2012). For example, the IARC system separately evaluates and rates the human, animal, and mechanistic/other data before integrating these three types of evidence into one overall classification. On the other hand, the IOM reports on Agent Orange did not separately evaluate and then integrate these three types of evidence into one overall classification. Instead, IOM based the assessment of evidence on the epidemiological studies and used toxicological and mechanistic information to assess biological plausibility (IOM 2008). Although classification schemes and methods differ across these agencies, these differences do not necessarily result in different conclusions concerning the evidence for causality.

Because the focus of ATSDR's assessment was primarily on the epidemiological evidence, and non-cancers as well as cancers were assessed, the approach used by the IOM to assess evidence for causation was most appropriate. However, the IOM used a different classification scheme for its Agent Orange reports than for its Gulf War reports (IOM 2008). Moreover, the Gulf War classification scheme has changed the definition of its categories (while retaining the names of the categories) over time.

The classification scheme adopted for this report is the one recommended by an IOM panel that reviewed the VA's presumptive disability decision-making process for veterans (IOM 2008). This scheme makes clear when the evidence for causality is "at least as likely as not" or at the level of "equipoise and above." ATSDR adopted this scheme because of its focus on the epidemiological evidence for causation (i.e., there is no category for evidence of a statistical association). Additionally, the scheme is one that is already in use by the U.S. Department of Veterans Affairs (VA) in its decision-making concerning compensation for service-related disability compensation claims. The issue of compensation has been of major concern for the Camp Lejeune community. The classification scheme uses four categories:

1. Sufficient: The evidence is sufficient to conclude that a causal relationship exists.

2. Equipoise and Above[1]: The evidence is sufficient to conclude that a causal relationship is at least as likely as not, but not sufficient to conclude that a causal relationship exists.

3. Below Equipoise: The evidence is not sufficient to conclude that a causal relationship is at least as likely as not, or is not sufficient to make a scientifically informed judgment.

4. Against: The evidence suggests the lack of a causal relationship.

The IOM panel anticipated that if the evidence for causation was categorized as "sufficient" or as "equipoise and above," then the VA would consider a presumptive service connection based on the causal evidence. If the evidence for causation was categorized as "below equipoise," then the VA might reconsider the evidence at a later date as more research becomes available. This approach would be in agreement with VA policy to give the benefit of the doubt to the veteran (IOM 2008).

Classification scheme categories

Sufficient evidence for causation: the evidence is sufficient to conclude that a causal relationship exists. This category would be met, for example, if:

1. There is sufficient evidence from human studies in which chance and biases (including confounding) can be ruled out with reasonable confidence, **or**

2. There is less than sufficient evidence from human studies but sufficient evidence in animal studies and strong evidence that the agent acts through a relevant mechanism in humans.

Sufficient evidence from human studies can be provided by a meta-analysis and/or by several studies considered to have high utility.

Considerations in assessing the evidence include several of Hill's viewpoints: (1) temporal relationship, (2) consistent positive associations (e.g., risk ratio or odds ratio greater than 1.1), (3) magnitude of the effect estimate (e.g., risk ratio, odds ratio), (4) exposure-response relationship, and (5) biological plausibility (Hill 1965).

Equipoise and above evidence for causation: The evidence is sufficient to conclude that a causal relationship is at least as likely as not, but not sufficient to conclude that a causal relationship exists. This category would be met, for example, if:

1. The degree of evidence from human studies is less than sufficient but there is supplementary evidence from animal studies and/or mechanistic studies that supports causality, **or**

[1] In an earlier draft of this document, the category "Modest evidence for causation" was created and used to characterize evidence that was above equipoise but less than sufficient to conclude that a causal relationship existed.

2. A meta-analysis does not provide convincing evidence (e.g., the summary risk estimate is close to the null value of 1.0, i.e., ≤1.1), or if the meta-analysis observes a non-monotonic exposure-response relationship) but there is at least one epidemiological study considered to be of high utility occurring after the meta-analysis has been conducted, in which an association between the exposure and increased risk of the disease of interest has been found and in which chance and biases can be ruled out with reasonable confidence.

3. A meta-analysis has not been conducted, but there is at least one epidemiological study considered to be of high utility in which an association between the exposure and increased risk of the disease of interest has been found and in which chance and biases can be ruled out with reasonable confidence.

Below Equipoise evidence for causation: The evidence is not sufficient to conclude that a causal relationship is at least as likely as not, or is not sufficient to make a scientifically informed judgment. This is a rather broad category that encompasses:

- evidence sufficient to conclude an association exists but where there is some doubt that biases can be ruled out and the animal and mechanistic evidence is weak, or
- evidence for an association that is so limited that there is substantial doubt that biases can be ruled out, or
- insufficient evidence to determine whether an association exists.

Evidence against a causal relationship: The evidence suggests the lack of a causal relationship.

ATSDR's Methods Used to Assess the Strength of the Evidence for Causation

Comprehensive assessments of the evidence for causation for TCE, PCE, vinyl chloride and benzene have been conducted by IARC (IARC 97, 2008; 100F, 2012; 106, 2014), EPA (EPA 2011, 2012), and NTP (NTP 2015). ATSDR placed high weight on these assessments in reaching its conclusions concerning the evidence of causation for these chemicals and the diseases evaluated in these reports. ATSDR also placed high weight on the results of recent meta-analyses that were conducted by EPA (Scott and Jinot 2011) and other researchers (e.g., Karami et al. 2012, 2013; Vlaanderen et al. 2011, 2012, 2014). Meta-analyses were valuable for evaluating occupational studies. Many of these studies lacked precision in their effect estimates, in particular, when exposure-response trends were evaluated, due to small numbers of exposed with the disease of interest. Moreover, some of the meta-analyses were able to reduce the inconsistencies in findings across studies by taking into account study differences in exposure levels and in the quality of exposure assessments. Some of the meta-analyses also evaluated whether confounding bias, publication bias and between-study heterogeneity was a concern. Also given high weight were studies considered to be of high or moderate utility by NTP in its evaluation of TCE and kidney cancer, non-Hodgkin lymphoma and liver cancer (NTP 2015). These studies are identified in the tables for these diseases.

Epidemiological studies that were published after a meta-analysis was completed were included in the tables and evaluated in the assessment. Also assessed and included in the tables were all studies that evaluated exposure-response trends even if they were included in a meta-analysis. For these studies, the assessment focused on the results of the exposure-response analyses. Although not included in the tables, the assessment also considered information from animal studies and mechanistic information that was reported in the EPA, IARC and NTP reports, epidemiological studies, and epidemiological review articles.

In its assessment of each contaminant and disease, ATSDR highlighted epidemiological findings (i.e., effect estimates such as risk ratios, odds ratios, standardized mortality ratios and standardized incidence ratios) that:

1. Represented the risks to those most likely to have been exposed (and possibly less affected by exposure misclassification bias), such as effect estimates in the higher cumulative exposure or exposure intensity categories, higher probability of exposure categories, and higher duration of exposure categories, based on semi-quantitative or quantitative exposure assessments;

2. Minimally affected by healthy worker effect biases; and

3. Minimally affected by confounding bias due to smoking or other risk factors.

Also highlighted were findings from the evaluation of disease subgroupings (e.g., leukemia types) and findings from the evaluation of effect modification (e.g., analysis of possible susceptible populations such as those with a genetic polymorphism affecting a key metabolic pathway for the chemical under evaluation). For cancers with a high probability of survival, findings based on incidence data were highlighted because mortality data has several limitations including: (1) cancers may be missed if the exposure causes a less fatal form of the disease or if the cancer is not an underlying or contributing cause of death; and (2) cancer information provided by cancer registries (e.g., histological information and identification of primary and metastatic sites) has greater accuracy compared to the information available from the death certificate, therefore disease misclassification should be reduced for findings based on incidence data.

In the disease-specific tables, 95% confidence intervals were provided in order solely to indicate the level of precision or uncertainty in the effect estimates. An effect estimate (e.g., risk ratio, odds ratio, or standardized mortality ratio) was considered to have good precision (or less uncertainty) if the ratio of the upper limit to lower limit of its 95% confidence interval was ≤ 2.

In our assessment, we did not use confidence intervals to determine whether a finding was “statistically significant” nor did we use significance testing to assess the evidence for causality (Rothman et al. 2008). There are several limitations to the use of statistical significance testing (Rothman et al. 2008, Goodman 2008, Stang et al 2010). Moreover, a finding that does not achieve statistical significance nonetheless can provide important evidence for a causal association, while a finding that achieves statistical significance can often lack scientific and public health significance. Because of the limitations of statistical significance testing, it was not used to assess the epidemiological evidence. Instead, ATSDR assessment of the epidemiological evidence considered some of the viewpoints associated with

Hill: (1) temporal relationship, (2) magnitude of the effect estimate (e.g., risk ratio, odds ratio, and standardized mortality ratio), (3) consistency of findings, (4) exposure-response relationship (although the relationship could be non-linear or non-monotonic), and (5) biological plausibility (Hill 1965). When considering the magnitude of the effect estimate, an effect estimate was considered "near the null value" if ≤1.10 and "elevated" if >1.10. Also considered were the effects of biases, in particular exposure misclassification, healthy worker effect, and confounding.

1. Impact of Bias

Biases impact the validity of a study. Therefore, a consideration in the assessment of the evidence for causation was the impact of key biases on the findings of the studies. The key limitation of all the studies was **exposure misclassification**. The impact of exposure misclassification bias would likely be to bias dichotomous comparisons (e.g., exposed vs unexposed) towards the null if an effect of the exposure is truly present, and to distort exposure-response trends (e.g., the curve may flatten or attenuate at high exposure levels). It is possible for exposure misclassification bias to be "differential" (i.e., the bias is associated both with exposure and disease status). If differential, dichotomous comparisons can be biased toward or away from the null. For example, if exposures are assessed retrospectively (e.g., when cases and controls are interviewed about their past exposures), it is possible for exposure misclassification bias to be differential. However, differential exposure misclassification is not likely for studies that assess exposures via job-exposure matrices (JEMs), plant record reviews, exposure biomonitoring, or that historically reconstruct exposures via modeling.

The vast majority of the epidemiological studies that evaluated the health effects of TCE, PCE or vinyl chloride were occupational studies. Some of the occupational studies used semi-quantitative JEMs specific to a plant or industry to assess exposures. The JEMs were developed based on plant records, literature data, expert judgment from industrial hygienists, and/or exposure measurements (e.g., biomonitoring or work area sampling). Some studies used generic JEMs that linked a wide range of occupations and industries to exposure metrics for exposures of interest. All JEMs may introduce exposure misclassification bias because they assume that workers with the same job during a specific time period will have similar exposures. However, generic JEMs are likely to result in much greater exposure misclassification bias than industry-specific or plant-specific JEMs. Occupational studies that did not use JEMs based their exposure assessments on reviews of work history information (e.g. obtained via interview or from plant records) by experts in industrial hygiene. The quality of expert-assessed exposure levels depends on the amount and accuracy of the available information for the jobs being assessed. A few studies based their assessment of TCE exposure on urine trichloroacetic acid (TCA) measurements. However, urine TCA is not specific to TCE exposure and measures recent exposures that may not reflect exposures occurring in the past. Drinking water studies included in this review based their exposure assessments on modeled historical estimates of contaminant levels in the drinking water serving residences or workplaces. Information on the amount of water consumed by individuals was either limited (due to likely inaccuracies in the recall of past consumption habits) or unavailable.

Another important bias is due to the **Healthy worker/veteran effect**. This bias likely occurred in studies that compared incidence or mortality rates in worker or veteran cohorts with rates in the general population (Checkoway et al. 2004, McLaughlin et al. 2008, Kirkeleit et al. 2013). Such a bias would tend to produce underestimates of the effect of exposure, and in many situations, reduce measures of association (e.g., SIR or SMR) below the null value. Other selection biases such as loss to follow-up in

cohort studies or bias in the selection of cases or controls in case-control studies were generally minimal for most of the studies evaluated in this assessment.

2. Confounding assessment

Another issue for most of the studies is possible **confounding** due to co-exposures to other workplace or environmental chemicals. For example, dry cleaning workers employed before the early 1960s were likely exposed to other solvents besides PCE. Dry cleaning workers also used solvents for spot removal although these exposures would be considerably lower than exposures to the primary solvent. Workers in aircraft manufacturing or maintenance may have been exposed to TCE, PCE and other solvents. In the Camp Lejeune studies (Bove et al. 2014a, b) and the NJ drinking water studies (Cohn et al. 1994, Bove et al. 1995), both TCE and PCE appeared together as drinking water contaminants. However, the possibility of confounding occurs only if the co-exposure independently increases the risk of the disease under evaluation in addition to being correlated with the exposure of interest.

An additional concern was the possibility of confounding by non-occupational and non-environmental risk factors for the diseases under evaluation, such as smoking and alcohol consumption. However, for appreciable confounding (e.g., a change in the effect estimate by >20%) by smoking or any other risk factor to occur, at least two requirements must be met: (1) the risk factor must have an association with the outcome of interest at least as strong as the exposure of interest, and (2) the risk factor must also have a strong association with the exposure of interest. For the latter requirement to be met, the prevalence of the risk factor must be very different in the compared groups. This might occur for example when a worker (or veteran) cohort is compared to the general population. However, the prevalence of risk factors (other than the exposure of interest) should be similar when comparisons are made either internal to a cohort or between similar cohorts (e.g., similar workforces or similar military personnel), and therefore confounding would be expected to be minimal for these comparisons.

In general, substantial confounding due to smoking or any other risk factor is rare in occupational and environmental epidemiology. Even for studies of an occupational or environmental exposure and lung cancer, a summary measure (e.g., RR, OR) adjusted for smoking rarely differs by more than 20% from the unadjusted summary measure (Blair et al. 2007). In any case, the amount of bias due to confounding will not be greater than the weaker of these two associations: (1) between the exposure of interest and the confounder; (2) between the confounder and the disease of interest (Smith and Kriebel 2010).

Many of the studies included in the meta-analyses or listed in the tables did have information on smoking and were able to adjust for smoking if confounding was present. Most of the studies that did not have information on smoking were able to indirectly assess whether confounding due to smoking affected the results by evaluating whether a smoking-related disease that was not known to be associated with the exposure of interest was elevated in the study. Another indirect approach to evaluate possible confounding due to smoking would be to evaluate all smoking-related diseases in the study for which the risk from smoking is known (or expected to be) much larger than the risk from the exposure of interest. If appreciable confounding due to smoking were present, one would expect that all these diseases would be elevated for the exposure of interest.

Many of the studies evaluated, or adjusted for, risk factors in addition to smoking such as alcohol consumption and socioeconomic status. The appendix lists the studies included in the tables, whether or not they evaluate smoking as a possible confounder, and any additional potential confounders.

Assumptions on Duration of Exposure

One objective of this report was to evaluate whether there was sufficient information in the scientific literature to determine a minimum duration at Camp Lejeune, or a minimum level of exposure, necessary to increase the risk of one or more of the diseases being assessed. The 2012 Honoring America's Veterans and Caring for Camp Lejeune Families Act established a minimum duration at Camp Lejeune of 30 days in order to be eligible for health benefits under the Act. It is unclear how the minimum duration was established for this legislation. However, the evidence from the epidemiological studies included in this assessment is not sufficient to contradict this minimum duration. Moreover the results from the Camp Lejeune mortality studies suggest that a 30 day minimum duration requirement may be appropriate since elevated risks for some of the diseases evaluated were observed for exposure durations of 1-3 months. These results should not be surprising given that the levels of TCE, PCE and vinyl chloride measured or estimated in the drinking water systems at Camp Lejeune considerably exceeded their respective MCLs.

The studies evaluated in this report provide very limited information concerning the level or duration of exposure associated with an increased risk of a cancer or other disease. For example, those studies that evaluated cumulative exposure or exposure duration often used wide categorizations (e.g., duration of exposure > 0 to 5 years). An additional interpretative difficulty is the possible inverse relationship between duration and exposure intensity, e.g., high exposure intensities may require only a short duration of exposure whereas low exposure intensities may require longer exposure durations. Although cumulative exposure is a useful metric, it obscures this interplay between duration and intensity. Specifying a minimum duration of exposure also presupposes that there is a known threshold amount of exposure below which there is no excess risk. However, there is no compelling evidence that such thresholds exist for these contaminants and the cancers and other diseases evaluated in this report.

For cardiac birth defects, it is possible that very short durations of exposure to the mother may be sufficient if the exposure occurs during the relevant vulnerability period for cardiac defects, i.e., 3-9 months gestation. In-utero exposures have been associated with increased risk of childhood leukemia (Costas et al. 2002).

Given that sufficient evidence for a threshold is lacking, ATSDR recognizes that a decision to establish a specific minimum exposure duration for policy purposes will primarily be based on social, economic and legal factors.

Presentation of Findings

An overall summary table is provided that lists each disease and ATSDR's assessment of the evidence of causality for each chemical. In addition, a table for each disease was created followed by a narrative that includes the assessment of the evidence for each chemical and ATSDR's conclusions. Each disease-specific table first lists the results from meta-analyses that have been conducted. Next, the table lists the results from epidemiological studies that: (1) were not included in meta-analyses because they appeared after the meta-analyses were conducted; and/or (2) contained information on exposure-response trends (e.g., cumulative exposure, exposure duration, employment duration, exposure intensity, probability of exposure, or exposure biomarker); and/or (3) are included because no meta-analysis has been conducted to date. The studies in most of the tables are grouped in the following manner: cohort studies of TCE and PCE exposures at industrial facilities, case-control studies of occupational exposures to TCE and PCE, studies of dry cleaning workers, vinyl chloride worker studies, benzene worker studies, and drinking water studies including the studies conducted at Camp Lejeune. (For some diseases there are too few studies of each category to group in this manner. For these tables, cohort studies are grouped together, then case-control studies, and then the drinking water studies.) Following each table, a summary of the conclusions for that disease from the reviews by EPA, IARC and NTP, if available, are provided, followed by ATSDR's assessment.

ATSDR's assessment includes a brief discussion of the meta-analyses and key studies. Animal study information from the reviews by IARC, EPA and/or NTP are also provided. If available, mechanistic information from animal or human studies specific to the disease and chemical under evaluation are also presented. A summary statement of the evidence is then provided.

In an appendix, a table is provided listing each study and information concerning possible confounding by smoking as well as information on whether other key risk factors were assessed or adjusted for.

Overall Summary of the Evidence*

Disease	Chemicals	Meta-analysis Citations	ATSDR Conclusions
Kidney Cancer	TCE	Kelsh 2010; Scott (EPA) 2011; Karami (NCI) 2012	Sufficient evidence for causation
	PCE		Below equipoise evidence for causation
Non-Hodgkin Lymphoma	TCE	Kelsh 2010; Scott (EPA) 2011; Karami (NCI) 2013	Sufficient evidence for causation.
	PCE		Equipoise and above evidence for causation
	Benzene	Steinmaus 2008; Kane 2010; Vlaanderen 2011	Sufficient evidence for causation
Multiple Myeloma	TCE	Alexander 2006; Karami (NCI) 2013	Equipoise and above evidence for causation
	PCE		Below equipoise evidence for causation
	Benzene	Infante 2006; Vlaanderen 2011	Equipoise and above evidence for causation
Leukemias	TCE	Alexander 2006; Karami (NCI) 2013	Equipoise and above evidence for causation for all types of leukemia
	PCE		Below equipoise evidence for causation
	Benzene	Khalade 2010; Vlaanderen 2011; Vlaanderen 2012	Sufficient evidence for causation for all types of leukemia
	Vinyl chloride	Boffetta 2003	Below equipoise evidence for causation
Liver Cancer	TCE	Alexander 2007; Scott (EPA) 2011	Equipoise and above evidence for causation
	PCE		Below equipoise evidence for causation
	Vinyl chloride	Boffetta 2003	Sufficient evidence for causation
	Benzene		Below equipoise evidence for causation
Pancreatic Cancer	TCE	Ojajarvi 2001, 2007	Below equipoise evidence for causation
	PCE	Ojajarvi 2001, 2007	Below equipoise evidence for causation
	Benzene		Below equipoise evidence for causation
	Vinyl chloride	Ojajarvi 2001, 2007	Below equipoise evidence for causation
Prostate Cancer	TCE	Morgan 1998	Below equipoise evidence for causation
	PCE		Below equipoise evidence for causation
	Vinyl chloride		Below equipoise evidence for causation
Breast Cancer (male & female)	TCE		Below equipoise evidence for causation
	PCE		Below equipoise evidence for causation
	Benzene		Below equipoise evidence for causation

Disease	Chemicals	Meta-analysis Citations	ATSDR Conclusions
Bladder Cancer	TCE		Below equipoise evidence for causation
	PCE	Vlaanderen (IARC) 2014	Sufficient evidence for causation
	Vinyl chloride		Below equipoise evidence for causation
	Benzene		Below equipoise evidence for causation
Parkinson Disease	TCE		Equipoise and above evidence for causation
	PCE		Below equipoise evidence for causation
Kidney Diseases	TCE		Equipoise and above evidence for causation for end-stage renal disease
	PCE		Equipoise and above evidence for causation for end-stage renal disease
Esophageal Cancer	TCE		Below equipoise evidence for causation
	PCE		Below equipoise evidence for causation
	Benzene		Below equipoise evidence for causation
Rectal Cancer	TCE		Below equipoise evidence for causation
	PCE		Below equipoise evidence for causation
Brain/CNS Cancers	TCE		Below equipoise evidence for causation
	PCE		Below equipoise evidence for causation
	Vinyl chloride	Boffetta 2003	Below equipoise evidence for causation
Systemic Sclerosis/ Scleroderma	TCE	Cooper 2009; Zhao 2016	Equipoise and above evidence for causation
	PCE	Zhao 2016	Below equipoise evidence for causation
	Benzene	Zhao 2016	Below equipoise evidence for causation
Cardiac Defects	TCE		Sufficient evidence for causation
	PCE		Below equipoise evidence for causation

[*] The evidence for a causal association between each exposure and disease is presented in more detail in the following tables and accompanying text.